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Disruptive effects of prefeeding and haloperidol administration on multiple measures of food-maintained behavior in rats

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Abstract

Four rats responded under a choice reaction-time procedure. At the beginning of each trial, the rats were required to hold down a center lever for a variable duration, release it following a high- or low-pitched tone, and press either a left or right lever, conditionally on the tone. Correct choices were reinforced with a probability of .95 or .05 under blinking or static houselights, respectively. After performance stabilized, disruptive effects of free access to food pellets prior to sessions (prefeeding) and intraperitoneal injection of haloperidol were examined on multiple behavioral measures (i.e., the number of trials completed, percent of correct responses, and reaction time). Resistance to prefeeding depended on the probability of food delivery for the number of trials completed and reaction time. Resistance to haloperidol, on the other hand, was not systematically affected by the probability of food delivery for all dependent measures.

Keywords

Behavioral momentum theory; Choice reaction-time procedure; Haloperidol; Lever press; Prefeeding; Rats

1. Introduction

Resistance to change is a measure of behavioral persistence when disruptive events are introduced. In a prototypical study (e.g., Nevin, 1974), the schedule components differed in terms of reinforcement rates. Resistance to change, as expressed by performance during disruption relative to that during baseline, is typically greater in the component with higher reinforcement rates. This finding, replicated in a wide variety of studies using different procedures, has led to the development of behavioral momentum theory (Nevin, 1992).

A challenge to behavioral momentum theory comes from studies examining effects of pharmacological disruptors. Although some researchers (e.g., Egli et al., 1992; Harper, 1999a, 1999b; Hoffman et al., 1987; Poling et al., 2000; Yoo et al., 2003) have obtained results consistent with behavioral momentum theory with drugs from several pharmacological classes such as stimulant (e.g., cocaine), antipsychotic (e.g., haloperidol), and opioid (e.g., morphine), others have found that pharmacological disruptors do not

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operate in the same manner as non-pharmacological disruptors (e.g., Cohen, 1986; Jimenez-Gomez and Shahan, 2007; Lamb and Ginsburg, 2005; Pinkston et al., 2009). For example, Cohen (Experiment 3) investigated resistance of food-maintained responses by rats to *d*-amphetamine, sodium pentobarbital, haloperidol, and cholecystokinin, and found that behavior was not necessarily more resistant to disruptive effects of these drugs in the component with higher reinforcement rates.

It is important to note that, except for Yoo et al. (2003), previous studies have measured resistance to pharmacological disruptors on response rates. Drugs of various classes can affect some dimensions of behavior and not others (e.g., Blokland and Honig, 1999); thus, resistance to disruption may manifest itself in other measures. To account for the aforementioned discrepant data sets, it is worthwhile to examine effects of pharmacological disruptors on multiple behavioral measures to better characterize their effects.

Yoo et al. (2003) showed that disruption of both response rate and conditional discrimination accuracy by the atypical antipsychotic resperidone was greater under the leaner reinforcement condition in a woman with intellectual disabilities. Along with this study, one possible behavioral measure of interest is conditional discrimination accuracy. The use of this measure not only extends the scope of behavioral momentum theory to something other than response rates (Nevin et al., 2003), but also allows us to detect degradation in stimulus control caused by drug administration that could obscure effects of differential stimulus–reinforcer relations on resistance to change (e.g., Harper, 1999a, 1999b).

Another possible measure is reaction time. Brockel and Fowler (1995) examined disruptive effects of haloperidol on reaction time in rats and found that reaction time increased as a function of the doses of haloperidol administered. This suggests that reaction time can be a useful measure to examine disruptive effects of haloperidol in the context of behavioral momentum theory.

The purpose of this study was twofold: (1) to develop a procedure with multiple behavioral measures that are sensitive to disruptive effects of environmental manipulations (e.g., prefeeding) and (2) to investigate whether haloperidol disrupts food-maintained behavior in the same manner as a non-pharmacological disruptor. Haloperidol, a typical antipsychotic, was chosen based on its disruptive effects on reaction time reported in Brockel and Fowler (1995). Three behavioral measures were employed: conditional discrimination accuracy, reaction time, and the number of trials completed in a session.

2. Materials and methods

2.1. Subjects

Four male Sprague-Dawley rats, each experienced with a reaction-time task (Blokland, 1998), were maintained at 85% (±5%) of their predicted free-feeding body weights based on the procedure described by Davenport and Goulet (1964). They were housed individually in a temperature-controlled room with a 12:12 h light/dark cycle. The National Institute for Occupational Safety and Health (NIOSH) animal facility is specific-pathogen free,

environmentally controlled, and accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International. All animal procedures have been reviewed and approved by the NIOSH Animal Care and Use Committee.

2.2. Apparatus

Experimental sessions were conducted in four standard operant-conditioning chambers 22 cm high, 29 cm wide, and 24 cm deep. On the front panel of the chamber were two retractable levers 7 cm above the grid floor. Two white cue lights were positioned above each lever. Between the two levers were a response lever and a rectangular opening centered 8.5 cm above the floor. Food pellets (45 mg, Research Diets) were dispensed into the opening. A click sound accompanied each pellet delivery. A photocell detected the rat's head in the opening. General illumination was provided by a house light positioned at the rear of the chamber. High- (10 kHz; 90 dB) and low-pitched (2.5 kHz; 90 dB) tones were presented from a speaker positioned at the back panel of the chamber. Experimental events were controlled and recorded by MED-PC® (Version 4.0) for Windows® software and interfacing.

2.3. Procedure

2.3.1. Baseline—Sessions usually were conducted 5 days per week at approximately the same time each day. A trial began with the illumination of the houselight that was either static or blinking at 0.2 s interval. The rats were required to hold down the center lever for a variable duration, ranging from 0.6 to 1.5 s (with steps of 0.1 s; chosen randomly without replacement), until the presentation of a high-or low-pitched tone. If the rats released the center lever after 0.2 s and before 1.5 s had elapsed since the presentation of the tone, the tone was turned off, the left and right levers were inserted, and the cue lights above the levers were turned on. If the rats released the lever before 0.2 s or after 1.5 s had elapsed, on the other hand, there was no programmed consequence, and the trial was repeated. These arrangements were made to exclude invalid responses with too short or too long latencies (cf. Blokland, 1998). A trial was also repeated if the rats released the lever before the tone. Following the insertion of the levers, a response to the left or right lever delivered a food pellet intermittently following the high- or low-pitched tone, respectively. On trials with the blinking houselight, a food pellet was delivered with a probability of .95 (hereafter rich condition). On trials with the static houselight, the probability of reinforcement was .05 (lean condition). A 10-s intertrial interval interspersed between trials during which the chamber was dark and the side levers were retracted.

High- and low-pitched tones were quasi-randomly presented with the restrictions that both tones were presented equally often in each reinforcement condition and that the same tone was presented on no more than three consecutive trials. Rich and lean conditions alternated regularly after eight trials, with the initial condition in a session determined randomly. A session lasted until 80 trials were completed or until 60 min had elapsed, whichever occurred first. The performance was considered as stable if there was no upward or downward trend in the three dependent measures during the last 5 sessions, as judged by visual inspection.

2.3.2. Resistance to change tests—Two resistance-to-change tests were conducted. First, rats were fed in their home cage 60 min prior to the session for 3 consecutive days (prefeeding). They were given 5% of their body weight in food pellets (20.8, 23.5, 21.1, and 22.6 g of food for Rats 17–20, respectively). Second, rats were given a 0.03, 0.06, or 0.12 mg/kg intraperitoneal injection of haloperidol 1 h prior to the session. Haloperidol was dissolved into an acidified saline vehicle to an injection volume of 1.0 ml/kg. Each haloperidol session was proceeded by a session in which only the saline vehicle was injected (hereafter saline session) and was followed by at least one no-injection session. The three doses were administered in an ascending order. Rat 20 did not receive the dose of 0.12 mg/kg of haloperidol. All procedural details were the same as in the baseline condition, except that a tone was presented if rats failed to meet the lever-hold response requirement in 120 s and that the side levers were retracted if no side lever response was made in 20 s.

3. Results and discussion

Fig. 1 shows the performance during the baseline and saline sessions preceding the disruption tests. Except for the saline sessions for Rats 17 and 19, there was no systematic difference in the number of trials completed between the two reinforcement conditions. Accuracy was higher and reaction time was shorter under the rich components, with some exceptions on reaction time in Rats 17 and 19.

The upper panel of Fig. 2 shows the results of the prefeeding test, expressed as log proportion of the mean of the last five baseline sessions. Reaction time is expressed as a reciprocal such that a larger value indicates less disruption. With the exception of reaction time in Rat 20, resistance to change of the number of trials completed and reaction time was greater under the rich condition, demonstrating sensitivity of these two measures to prefeeding. There was no systematic difference in resistance to change of percent correct, except that Rat 19 showed greater resistance to change under the rich condition.

The lower panel of Fig. 2 shows the results of the haloperidol test, expressed as log proportion of the mean of the three saline sessions. For Rats 17 and 19, the third data points for percent correct and reaction time were plotted only when at least one component was completed in both rich and lean conditions. Haloperidol administration greatly disrupted the number of trials completed only in Rats 17 and 19. In these rats, however, no differential resistance to haloperidol was observed in all dependent measures, with the exception that resistance to change of reaction time was somewhat greater under the rich condition in Rat 17.

These results show that resistance to prefeeding depended on the probability of food delivery with the number of trials completed and reaction time, whereas resistance to haloperidol was not systematically affected by the probability of food delivery with all dependent measures. This is consistent with previous studies in which pharmacological disruptors did not operate in the same manner as non-pharmacological disruptors (e.g., Pinkston et al., 2009). Nevertheless, caution should be used when interpreting the results. First, the sample size was small (n = 4). Second, given the selected dose of haloperidol, which ranged from 0.03 to 0.12 mg/kg, disruptive effects of haloperidol were observed only

with the number of trials completed in two rats (Rats 17 and 19). Although the results are suggestive that disruptive effects of haloperidol are not altered by the reinforcement conditions, the generality of this finding must be confirmed with further investigations.

It is important to note that disruptive effects of haloperidol on percent correct were negligible. Thus, it is possible that this measure could have been sensitive to the baseline reinforcer probability if it had been more disrupted. The lack of disruptive effects, however, indicates that stimulus control was not degraded by haloperidol administration (cf. Harper, 1999a, 1999b). Therefore, the lack of differential resistance to haloperidol of the number of trials completed cannot be accounted for by loss of stimulus control by the multiple-schedule signals.

As mentioned previously, some researchers have obtained results consistent with behavioral momentum theory, even using haloperidol as a disruptor (Harper, 1999a). As Pinkston et al. (2009) pointed out, “the literature provides no clear indications of the boundary conditions under which behavioral momentum will hold for pharmacological disruptors” (p. 244). To further understand this issue, our strategy to employ multiple behavioral measures should be useful: disruptive effects of a drug that affects multiple systems of the brain may be identified in some behavioral measures but not in others. In this sense, the novel finding that reaction time was sensitive to resistance to prefeeding is an important addition to the literature because it suggests that such a measure can be used to detect effects of pharmacological disruptors. The utilization of multiple behavioral measures for a drug that affects multiple systems of the brain should be a promising step toward the identification of the boundaries of behavioral momentum theory.

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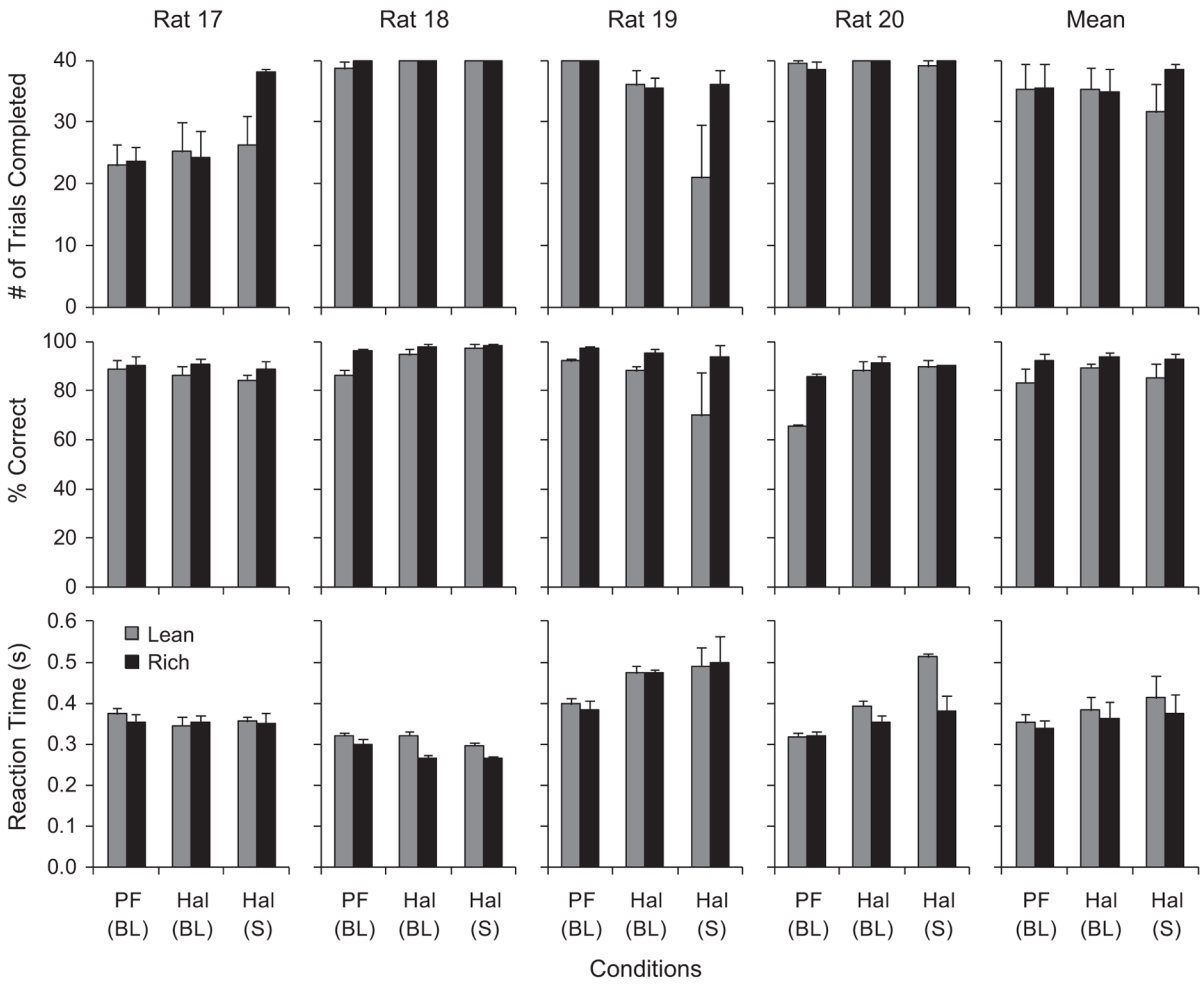

Fig. 1.

Mean number of trials completed (top panel), mean percent of correct responses (middle panel) and mean of median reaction times (bottom panel) during the baseline (BL) and saline (S) sessions preceding the prefeeding (PF) and haloperidol (Hal) tests. The baseline data are the average from the five sessions prior to the disruption test. The saline data are the average of the three sessions prior to each dose of haloperidol administration. The gray and black bars represent performance during the lean and rich conditions, respectively. The error bars represent the standard error of the mean.

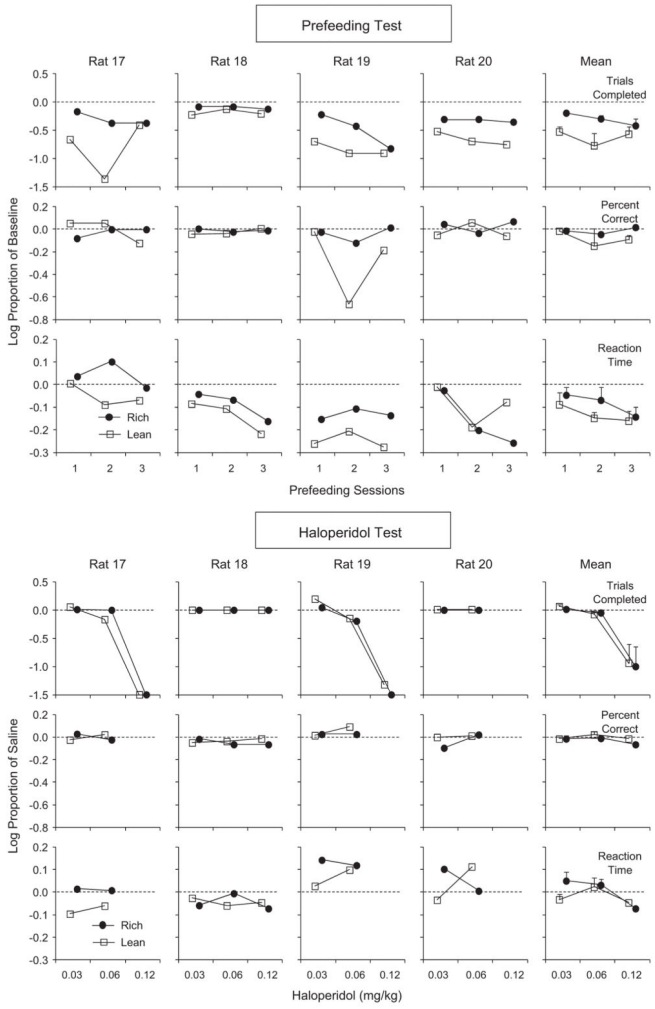

Fig. 2.

Upper panel: The number of trials completed (top row), percent correct (middle), and reaction time (bottom) expressed as log proportion of the mean of the five baseline sessions immediately prior to the prefeeding test as a function of prefeeding sessions. Reaction time is expressed as a reciprocal such that a larger value indicates less disruption. Closed circles and open squares represent the log proportion measures in the rich and lean conditions, respectively. The error bars in the group mean represent the standard error of the mean. Lower panel: The number of trials completed (top row), percent correct (middle), and reaction time (bottom) expressed as log proportion of the mean of the three saline sessions immediately prior to the haloperidol test as a function of dose in mg/kg. Because log proportion values cannot be calculated when no trial was completed at 0.12 mg/kg, the lowest value was set to −1.5. Note that the third data point of the group mean of percent correct and reaction time is composed of the data from a single subject. Other details are the same as in the upper panel.